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IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF :  
NAOHIKO HIROTA, ET AL. : EXAMINER: RAGHU  
SERIAL NO: 10/550,528 :  
FILED: NOVEMBER 27, 2006 : GROUP ART UNIT: 1652  
FOR: BARLEY LIPOXYGENASE 1 :  
GENE, METHOD OF SELECTING :  
BARLEY VARIETY, MATERIAL OF :  
MALT ALCOHOLIC DRINKS AND :  
PROCESS FOR PRODUCING MALT :  
ALCOHOLIC DRINK

**APPEAL BRIEF**

COMMISSIONER FOR PATENTS  
ALEXANDRIA, VIRGINIA 22313

SIR:

In accordance with 35 U.S.C. § 134, that the claims of the present application have been twice rejected, this brief is submitted in response to the rejections dated May 27, 2010 (“Action”).

**REAL PARTY OF INTEREST**

The real party of interest is Sapporo Breweries, Ltd, Tokyo, Japan.

**RELATED APPEALS AND INTERFERENCES**

To the best of Appellants' knowledge, there are no other appeals or interferences which will directly affect or be directly affected by, or have a bearing on, the Board's decision in this appeal.

**STATUS OF CLAIMS**

Claims 1-17 are active.

Claims 1-9 and 14-17 are rejected.

Claims 1-9 and 14-17 are appealed.

Claims 10-13 are allowed.

The appealed claims are presented in Appendix I.

**STATUS OF AMENDMENTS**

No outstanding amendments are present in this case.

**SUMMARY OF CLAIMED SUBJECT MATTER**

The invention claimed in the pending, rejected and appealed independent claims 1 and 3 with reference to exemplary support in the originally filed application is:

1. An isolated barley lipoxygenase-1 mutant gene, wherein the guanine at the splicing donor site (5'-GT-3') of the 5th intron of the barley lipoxygenase-1 gene is not guanine. *[page 8, lines 13-19]*

3. A selection method for barley lipoxygenase-1 deficient barley, the method comprising determining the presence or absence of a guanine at the splicing donor site of the 5th intron of the barley lipoxygenase-1 gene, and selecting the barley having an adenine, thymine or cytosine at the splicing donor site. *[page 9, lines 1-5]*

**GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL**

The first ground of rejection to be reviewed on appeal is of Claims 1-9 and 14-17 fulfill the legal requirements of written description under 35 U.S.C. § 112, first paragraph.

The second ground of rejection to be reviewed on appeal is of Claims 1-9 and 14-17 fulfill the legal requirements of enablement under 35 U.S.C. § 112, first paragraph.

There is an outstanding obviousness-type double patenting rejection over claims 7-9 and 14-17 of U.S. application serial no. 12/505,723. Appellate review of this rejection is NOT requested.

## **ARGUMENT**

### **1. Written Description**

This is an easy issue to decide made unduly complex by the Examiner.

Claim 1 recites (see Appendix I):

An isolated barley lipoxygenase-1 mutant gene, wherein the guanine at the splicing donor site (5'-GT-3') of the 5th intron of the barley lipoxygenase-1 gene is not guanine.

The non-mutated gene and its sequence (including structure of introns and exons) is known. This is not disputed. The Inventors of the present application have identified a beneficial mutant of this known gene that resides at the splicing donor site of the 5<sup>th</sup> intron. Introns and exons are well-known in the skilled person.

In the first instance, the Examiner cites to the Federal Circuit opinion in Regents of the Univ. of Cal. v. Eli Lilly as supportive of the rejection. Action at page 12. So it's worthwhile to assess what that case is about and what it is not about. In this case, the patent specification described a general method of producing human insulin cDNA, the amino acid sequences for the A and B chains of human insulin and further provided a protocol used to obtain rat insulin cDNA which was then used to express rat insulin to demonstrate that the protocol works.

The Federal Circuit held that the claims to human insulin cDNA require a precise definition "by structure, formula, chemical name or physical properties" of human insulin cDNA. Even though the application provided a description of a method of how to obtain human insulin cDNA and the amino acid sequences for the A and B chains of human insulin that are encoded by cDNA, the Federal Circuit held that the specification failed to provide a written description of human insulin cDNA. The description of rat insulin cDNA does not support the claim to human insulin cDNA. The Court stated that:

Written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name sufficient to distinguish it from other materials.

This decision is inapposite to the facts of the present case. Unlike the Regents of California, where the human gene that was claimed was not known, the barley (*Hordeum vulgare*) LOX-1 gene is known in the art (see paragraph [008] of the specification).

Indeed, subsequent Federal Circuit decisions has made it clear that in the context of the present case, LOX-1 has a known structure, which was within the knowledge of those skilled in the art, the specification and claims satisfy the written description requirement (see *Capon v. Eshhar* (Fed. Cir. 2005): “When the prior art includes the nucleotide information, precedent does not set a *per se* rule that the information must be determined afresh.”; see also *Falkner v. Inglis*, 79 USPQ2d 1001 (Fed. Cir. 2006): “Recitation of Known Structure Is Not Required” to satisfy written description requirement).

In the paragraph bridging pages 11-12 of the Action, the Examiner posits that (emphasis in original):

Claim 1-9 and 14-17 (as interpreted) are directed to any variant of mutant barley LOX-1 gene of undefined structure and a selection method for a barley comprising any variant or mutant LOX-1 gene/DNA and encoding a polypeptide with deficient LOX-1 activity. (“deficient” is a relative term and the term “deficient” is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention).

Taking each point, in turn:

- (1) Claim 1 is not directed to any variant or mutant barley LOX-1 gene but a mutant of a known gene having a known structure in which a guanine at a splice site is altered.

(2) Claim 1 does not state “deficient LOX-1 activity” so that statement is inapplicable to the claims as presented. Although as is discussed in the present specification at page 5, lines 9-14, the mutation of the guanine at the splicing donor site causes a loss of LOX-1 activity.

(3) Claim 3 recites selecting for barley that is deficient in LOX-1 activity in the preamble of the claim. The steps of that method involve determining the presence of a guanine at a particular location and then selecting those barley having a different base at that position. Initially, there is nothing wrong with the term “deficient” in the claims as a standard dictionary definition is --lacking in some necessary quality or element-- (see, e.g., <http://www.merriam-webster.com/dictionary/deficient>). Indeed, the specification, for example on page 5, lines 9-22 describes that the LOX-1 mutant having the base pair change at the splice donor the 5<sup>th</sup> intron lacks LOX-1 activity--notice the definition of deficient includes the term lacking and the specification describes lacking activity. As this is clearly described in the specification, e.g., on page 5, Applicants have shown possession of the claimed invention.

**2. Enablement**

As explained above in the context of the written description rejection, the structure of the barley LOX-1 gene is known.

Applicants have defined the mutant by sequence in that there is change at the donor splice site of the 5<sup>th</sup> intron. See page 5, lines 9-15. This mutant is deficient or lacks the endogenous activity of the LOX-1 protein.

As with the written description rejection, The examiner misinterpreted that the LOX-1 mutant encodes a polypeptide having diminished LOX-1 activity with some uncertain variable activity and that any variant or mutant barley LOX-1 gene of undefined structure encoding a polypeptide with undefined LOX-1 activity (enhanced or diminished) does not satisfy requirements of enablement.

However, the present invention relates to LOX-1 mutant genes encoding a polypeptide with loss of LOX-1 activity. This is demonstrated in paragraphs 0040, 0115, 0120 and Fig. 5 etc. that, in the LOX-1 mutant gene of the present invention, the 60th base G of the known barley LOX-I gene (SEQ ID NO: 1) is replaced by A (SEQ ID NO: 2). As bases 60-61 of SEQ ID NO: 1 constitute the splicing donor site (5-GT-3), this base substitution produces an aberration in LOX-1 splicing which results in a loss of LOX-1 activity. This is also described on page 5, lines 9-22.

Thus, a person skilled in the art would be able to make such a mutant, having the known LOX-1 mutant in hand and that with that mutation, regardless of other mutations in the gene, the resultant protein would lack or be deficient in LOX-1 activity based on the description of the present specification and common general technical knowledge.

Therefore, it would not constitute undue experimentation to make and use the claimed invention because the mutant that is defined in the claims (see Claim 1) and described in the specification is clearly and unambiguously identified and results in a loss of activity. This is

so because the tools for recombinant DNA manipulation are well-known to the skilled person and indeed are described throughout the specification and methods of determining the presence or absence of this mutation are well within the capabilities of the skilled person, particularly as the present specification provides extensive description of how to identify such a mutant.

**Conclusion**

For the reasons stated in this Brief, Appellants respectfully request that the Examiner's rejections be withdrawn with direction to allow all of the claims pending in this application and pass this case to issue.

Respectfully submitted,

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**APPENDIX 1 (CLAIMS)**

1. (Rejected) An isolated barley lipoxygenase-1 mutant gene, wherein the guanine at the splicing donor site (5'-GT-3') of the 5th intron of the barley lipoxygenase-1 gene-is not guanine.
2. (Rejected) The isolated barley lipoxygenase-1 mutant gene according to claim 1, wherein the base at the splicing donor site is adenine.
3. (Rejected) A selection method for barley lipoxygenase-1 deficient barley, the method comprising determining the presence or absence of a guanine at the splicing donor site of the 5th intron of the barley lipoxygenase-1 gene, and selecting the barley having an adenine, thymine or cytosine at the splicing donor site.
4. (Rejected) The selection method for barley lipoxygenase-1 deficient barley according to claim 3, comprising selecting the barley having an adenine at the splicing donor site.
5. (Rejected) The selection method for barley lipoxygenase-1 deficient barley according to claim 3 or 4, wherein the determining comprises
  - extracting genomic DNA from a barley sample,
  - amplifying a DNA fragment containing at least the splicing donor site of the 5th intron of the barley lipoxygenase-1 gene from the extracted genomic DNA, and
  - detecting the amplified DNA fragment by cleaving with a restriction enzyme to determine the presence or absence of guanine at the splicing donor of the 5<sup>th</sup> intron of the barley lipoxygenase-1 gene.
6. (Rejected) The selection method for barley lipoxygenase-1 deficient barley according to claim 5, wherein the restriction enzyme is AfalI, RsaI, or both.
7. (Rejected) A material for malt alcoholic beverages, wherein the material is selected from a group consisting of a seed, a malt, malt extract, barley decomposition product

or processed barley derived from barley, comprising the barley lipoxygenase-1 mutant gene according to claim 1 or 2.

8. (Rejected) A material for malt alcoholic beverages, wherein the material is selected from a group consisting of a seed, a malt, malt extract, barley decomposition product or processed barley derived from barley selected by the selection method according to claim 3.

9. (Rejected) A method for producing malt alcoholic beverages, the method comprising fermenting wort obtained from a seed, a malt, malt extract, barley decomposition product or processed barley derived from barley according to claim 7 or 8.

14. (Rejected) A seed, a malt, malt extract, barley decomposition product or processed barley derived from barley selected by the selection method according to claim 4.

15. (Rejected) A seed, a malt, malt extract, barley decomposition product or processed barley derived from barley selected by the selection method according to claim 5.

16. (Rejected) A seed, a malt, malt extract, barley decomposition product or processed barley derived from barley selected by the selection method according to claim 6.

17. (Rejected) A method for producing malt alcoholic beverages, the method comprising fermenting a seed, a malt, malt extract, barley decomposition product or processed barley derived from barley according to claims 14, 15, or 16.

**APPENDIX II (EVIDENCE)**

1. The present specification, referenced in the arguments presented in this brief.

**APPENDIX III (RELATED APPEALS AND INTERFERENCES)**

None.